REMARKS

INTRODUCTION:

In accordance with the foregoing, claims 16, 23 and 24 have been amended. No new matter is being presented, and approval and entry are respectfully requested.

Claims 16-25 are under consideration. Claim 26 is withdrawn. Reconsideration is respectfully requested.

REJECTION UNDER 35 U.S.C. §101:

In the Office Action, at pages 2-3, claims 16, 17, and 23-25 were rejected under 35 U.S.C. §101, for the reasons set forth therein. This rejection is traversed and reconsideration is requested.

Independent claim 16 has been amended to add the terminology: "and displaying by a display unit, the longest common subsequence (LCS) between the character sequence expressing the input amino acid sequence and the character sequence expressing the amino acid sequence having the optimum correspondence to the input amino acid sequence."

Independent claim 23 has been amended to add the terminology: "and a display unit to display the longest common subsequence (LCS) between the character sequence expressing the input amino acid sequence and the character sequence expressing the amino acid sequence having the optimum correspondence to the input amino acid sequence."

Independent claim 24 has been amended to add the terminology: "and displaying by a display unit, the longest common subsequence (LCS) between the character sequence expressing the input amino acid sequence and the character sequence expressing the amino acid sequence having the optimum correspondence to the input amino acid sequence."

The amendments to claims 16, 23, and 24 are supported, for example by p. 26, lines 12-33.

It is respectfully submitted that amended independent claims 16, 23 and 24 include a useful, tangible and concrete result. That is, displaying, by a display unit, the longest common subsequence (LCS) between the character sequence expressing the input amino acid sequence and the character sequence expressing the amino acid sequence having the optimum correspondence to the input amino acid sequence is a specific, substantial and credible result, sets forth a practical application of the invention that produces a real-world result, and can be substantially repeatable. The result is communicated to a practitioner of the instantly claimed invention. A physical transformation is performed in that the longest common

subsequence (LCS) between the character sequence expressing the input amino acid sequence and the character sequence expressing the amino acid sequence having the optimum correspondence to the input amino acid sequence is displayed by a display unit.

Therefore, it is respectfully submitted that amended independent claims 16, 23, and 24 provide a useful, tangible and concrete result and are patentable under 35 U.S.C. §101. Since claims 17 and 25 depend from amended claims 16 and 24, respectively, claims 17 and 25 are patentable patentable under 35 U.S.C. §101 for at least the reasons that amended claims 16 and 24 are patentable under 35 U.S.C. §101.

REJECTION UNDER 35 U.S.C. §112:

In the Office Action, at page 4-11, claims 16, 17, and 23-25 were rejected under 35 U.S.C. §112, second paragraph, for the reasons set forth therein. This rejection is traversed and reconsideration is requested.

A. The Examiner submitted that claims 16, 17, and 23-25 are indefinite under 35 U.S.C. §112, second paragraph, with respect to the terminology RMSD.

It is respectfully submitted that the arithmetic standard deviation is a statistic used to quantify the variability of a set of data calculated by subtracting the arithmetic mean from each data value individually, squaring the differences, summing the squares of the differences, dividing the sum of the squared differences by the total number of data values less one, and taking the square root of the quotient to produce the Root Mean Square Deviation, and the root mean square or standard deviation may, for example, be described mathematically as follows:

$$\sigma = \sqrt{\frac{\left(x_1 - \bar{x}\right)^2 + \left(x_2 - \bar{x}\right)^2 + ... + \left(x_N - \bar{x}\right)^2}{N}}$$

$$= \sqrt{\frac{d_1^2 + d_2^2 + ... + d_N^2}{N}}$$

$$= \sqrt{\frac{1}{N}\sum_{i=1}^{N}\left(x_i - \bar{x}\right)^2} = \sqrt{\frac{1}{N}\sum_{i=1}^{N}d_i^2}$$

At http://www.csse.monash.edu.au/hons/projects/2000/Edmund.Lam/thesis/node31.html, Root-Mean-Square Distance is defined as follows:

> The Root-Mean-Square distance is a commonly used scientific measure. It is a measure of the average squared error between a set of parameters.

$$RMS(\theta, \hat{\theta}) = \sqrt{\frac{1}{N} \sum_i^N (\theta_i - \hat{\theta}_i)^2} \qquad (60)$$

For the binomial distribution and univariate distributions in general, it simplifies to the absolute error between the estimates.

In the biological area, the RMSD is commonly known, for example, as a method in molecular modeling of measuring the difference, i.e., the distance difference, between different configurations of the same molecule (see http://big.mcw.edu/letter.php/R-7.html).

A molecule conformation generally has a set of 3-dimensional coordinates. Hence, in the present invention, to compare different molecules, to avoid distortion of the RMSD comparison, a molecule of a second substance represented by a point set $\{b_1,...,b_n\}$ is rotated with respect to a molecule of a first substance represented by a point set $\{a_1,...,a_m\}$, wherein a_k is related to b_k (k = 1,...,n), a rotation matrix U is applied to obtain Ub_k, and a root mean square distance is computed using:

$$r.m.s.d. = \frac{\left(\sum_{k=1}^{n} (w_k (Ub_k - a_k)^2)\right)^{\frac{1}{2}}}{n}$$

wherein: "The r.m.s.d. value is a value expressing a square root of a mean square distance between the corresponding elements constituting the substances" as is set forth on page 4, line 30 through page 5, line 1 of the specification.

Hence, it is respectfully submitted that the meaning of the term r.m.s.d, or alternatively, R.M.S.D., is clear and definite to one skilled in the art, and that amended independent claims 16, 23, and 24 are patentable under 35 U.S.C. §112, second paragraph, with respect to the terminology RSMD. Since claims 17 and 25 depend from amended claims 16 and 24, respectively, claims 17 and 25 are patentable under 35 U.S.C. §112, second paragraph, with respect to the terminology RSMD for at least the reasons amended claims 17 and 25 are patentable under 35 U.S.C. §112, second paragraph, with respect to the terminology RSMD.

B. The Examiner submitted that claims 16, 23 and 24 are indefinite under 35 U.S.C. §112, second paragraph, with respect to the terminology "determining spatially similar portions of substances by analyzing three-dimensional structures of a substance."

It is respectfully submitted that, for clarity, the following phrase of claim 16, referred to by the Examiner has been amended to recite:

determining spatially similar portions of substances <u>comprising amino acids</u> by analyzing three-dimensional structures of a substance by comparing a first probe structure expressed by three-dimensional coordinates of elements belonging to a first subset of a plurality of subsets of secondary structures of probe structures, the first subset comprising a first point set of an amino acid sequence database or a motif database and a ~~second~~-target structure expressed by three-dimensional coordinates of elements belonging to a second subset of a plurality of subsets of secondary structures of the target structure, the second subset comprising a second point set of an input amino acid sequence of the target structure (emphasis added)

Claims 23 and 24 have been amended in similar fashion.

It is respectfully submitted that amended claims 16, 23 and 24 are clear to one skilled in the art, and are now definite under 35 U.S.C. §112, second paragraph, with respect to the terminology "determining spatially similar portions of substances comprising amino acids by analyzing three-dimensional structures of a substance."

C. The Examiner submitted that claims 16, 23 and 24 are indefinite under 35 U.S.C. §112, second paragraph, with respect to the terminology "a first probe structure expressed by three-dimensional coordinates of elements belonging to a first probe subset of a plurality of subsets of secondary structure of probe structures, the first subset comprising a first point set of an amino acid sequence or a motif database."

It is respectfully submitted that, for example, the specification, page 53, lines 8-35 of the specification, recites:

> Therefore, described below are a method in which a set of elements constituting a molecule is divided into subsets based on the secondary structures, and the subsets are related to each other based on the similarities of spatial position relationships of elements that belong to the subsets, a method of evaluating similarities of spatial position relationships of a plurality of subsets that are related to one another, and a method of analysis by utilizing such methods.
>
> (1) Division of a point set into subsets.
>
> The structure A and the structure B are, respectively, constituted by a point set A = [a_1, a_2, a_3, ---, a_i, ---, a_m], where $1 \leq i \leq m$ and a point set B = [b_1, b_2, b_3, ---, b_j, ---, b_n], where $1 \leq j \leq n$, and each point is expressed by a three-dimensional coordinate consisting of a_i = (x_i, y_i, z_i) and b_j = (x_j, y_i, z_j).
>
> In order to facilitate determination of the correspondence among the points, the structure is divided into partial structures that are structurally meaningful, and a points set is divided into subsets. Examples of the partial structures which are structurally meaningful include functional groups and partial structures having certain functions in the case of chemical substances, and secondary structures such as helixes, sheets structures and partial structures developing certain functions in the case of proteins.

Hence, in the example described on pages 52-56 of the specification, a set of elements constituting a molecule is divided into subsets. This is what the subsets are subsets of. The subsets are related to each other based on the similarities of spatial position relationships of elements that belong to the subsets. Partial structures which are structurally meaningful include

functional groups and partial structures having certain functions in the case of chemical substances and secondary structures such as helixes, sheet structures, and partial structures developing certain functions in the case of proteins.

Thus, it is respectfully submitted that it is clear to one skilled in the art what "subsets" are subsets of.

Clearly, a plurality of probes are available for use to compare with the target structure.

The probe structures have a plurality of subsets selected as set forth above. A first point set is selected from an amino acid sequences database or a motif database. That is, the information intended to be included in the first point set of an amino acid sequence database or motif database includes point sets for functional groups and partial structures having certain functions in the case of chemical substances and secondary structures such as helixes, sheet structures, and partial structures developing certain functions in the case of proteins.

The target structure is expressed by a plurality of subsets obtained from an input amino acid sequence as explained above.

Thus, it is respectfully submitted that claims 16, 23 and 24 are clear to one skilled in the art and are definite under 35 U.S.C. §112, second paragraph, with respect to the terminology "a first probe structure expressed by three-dimensional coordinates of elements belonging to a first probe subset of a plurality of subsets of secondary structure of probe structures, the first subset comprising a first point set of an amino acid sequence or a motif database."

D. The Examiner submitted that claims 16, 23 and 24 are indefinite under 35 U.S.C. §112, second paragraph, with respect to the terminology "a second target structure expressed by three-dimensional coordinates of elements belonging to a second subset of a plurality of subsets of secondary structures of the target structure, the second subset comprising a second point set of an input amino acid sequence of the target structure."

Claims 16, 23 and 24 have been amended to change "a second target structure" to recite ---a target structure--- for clarity.

The terminology "a second probe subset" which the Examiner found unclear is not present in claims 16, 23 or 24. A word search revealed no hits. Hence, no change was made therein.

As noted above, in the example described on pages 52-56 of the specification, a set of elements constituting a molecule is divided into subsets. This is what the subsets are subsets of.

The target structures have a plurality of subsets selected as set forth above. A second point set is an amino acid sequence selected from the input amino acid sequence. That is, the information intended to be included in the second point set is an amino acid sequence.

Thus, it is respectfully submitted that claims 16, 23 and 24 are clear to one skilled in the art and are definite under 35 U.S.C. §112, second paragraph, with respect to the terminology "a second target structure expressed by three-dimensional coordinates of elements belonging to a second subset of a plurality of subsets of secondary structures of the target structure, the second subset comprising a second point set of an input amino acid sequence of the target structure."

E. The Examiner submitted that claims 16, 23 and 24 are indefinite under 35 U.S.C. §112, second paragraph, with respect to the terminology "dividing the second target structure into a plurality of second subsets based on secondary structures of the three-dimensional coordinates of the target structure."

Claims 16, 23 and 24 have been amended to change "second target structure" to recite ---target structure--- for clarity.

It is respectfully submitted that it is clear to those skilled in the art that the target structure has three-dimensional coordinates that are described by the plurality of second subsets. That is the secondary structures of the target structure are represented by a second subset of a plurality of subsets, wherein the second subset comprises a second point set of an input amino acid sequence of the target structure.

Thus, it is respectfully submitted that claims 16, 23 and 24 are clear to one skilled in the art and are definite under 35 U.S.C. §112, second paragraph, with respect to the terminology "dividing the target structure into a plurality of second subsets based on secondary structures of the three-dimensional coordinates of the target structure."

F. The Examiner submitted that claims 16, 23 and 24 are indefinite under 35 U.S.C. §112, second paragraph, with respect to reciting a step drawn to determining whether a correspondence is present between the first point set and the second point set by generating (I) generating a first tree structure for the first point set and a second tree structure for the second point set, (ii) pruning the second tree structure for the second point set, (iii) determining whether the first point set and the second point set have a same attribute, and (iv), if the first point set and the second point set have a same attribute, generating a correspondence between the first point set and the second point set, and with respect to the step of "determining whether a correspondence is present between the first point set of the probe structure and the second point set of the plurality of second subsets of the target

structure" together with "generating a correspondence between the first point set of the probe structure and the second point set of the plurality of second subsets of the target structure."

It is respectfully submitted that the terminology "attribute" is described in (4)-(6) on page 33, line 20 through page 37, line 25. The kinds of attributes are recited. Thus, the terminology "attribute" is submitted to be clear and definite to one skilled in the art.

It is respectfully submitted that the terminology "determining whether a correspondence is present between the first point set of the probe structure and the second point set of the plurality of second subsets of the target structure" is a global heading structure that recites that "determining" is taking place, wherein the global heading is followed by the terminology "by" to indicate that the operations recited thereafter (indented) are performed so that the final operation "generating a correspondence between the first point set of the probe structure and the second point set of the plurality of second subsets of the target structure" outputs what is determined. Thus, said terminology is submitted to be clear and definite to one skilled in the art.

Thus, it is respectfully submitted that claims 16, 23 and 24 are clear to one skilled in the art and are definite under 35 U.S.C. §112, second paragraph, with respect to the terminology "determining whether a correspondence is present between the first point set and the second point set by generating (i) generating a first tree structure for the first point set and a second tree structure for the second point set, (ii) pruning the second tree structure for the second point set, (iii) determining whether the first point set and the second point set have a same attribute, and (iv), if the first point set and the second point set have a same attribute, generating a correspondence between the first point set and the second point set, and with respect to the step of "determining whether a correspondence is present between the first point set of the probe structure and the second point set of the plurality of second subsets of the target structure" together with "generating a correspondence between the first point set of the probe structure and the second point set of the plurality of second subsets of the target structure."

G. The Examiner submitted that claims 16, 23 and 24 are indefinite under 35 U.S.C. §112, second paragraph, with respect to the terminology "calculating a root mean square distance (RMSD) between elements corresponding in the first point set of the probe structure and the second point set of the plurality of second subsets of the target structure to automatically determine a distance between the elements of the first point set and the elements of a second point set."

It is respectfully submitted that on page 5, lines 6-23, it recites:

For instance, it is assumed that there are substances expressed by a point set A = {a_1, a_2, ..., a_i, ..., a_m} and a point set B = {b_1, b_2, ..., b_j, ..., b_n}, wherein a_i (i = 1, 2, ..., m) and b_j (i = 1, 2, ..., n) are vectors expressing positions of the respective elements in the three-dimensional space. The elements constituting these substances A and B are related to each other, and the substance B is rotated and moved so that the r.m.s.d value between the corresponding elements is minimized. For example, if a_k is related to b_k (k = 1, 2, ..., n), the r.m.s.d value is obtained in the following equation (1) wherein U denotes a rotation matrix and W_k denote respective weights:

$$r.m.s.d. = \frac{\left(\sum_{k=1}^{n} (w_k(Ub_k - a_k)^2)\right)^{\frac{1}{2}}}{n} \quad \ldots (1)$$

Hence, it is respectfully submitted that it is clear to one skilled in the art that the terminology "element" refers to elements constituting the substances (see also, page 5, line 1 of the specification) and that the information included in a first and second point set is clear.

As noted above, in the biological field, the terminology RMSD is clearly understood by one skilled in the art to refer to a distance difference between different configurations of molecules, and does indeed result in a determination of an actual distance between corresponding elements from a first point set and a second point set.

Thus, it is respectfully submitted that claims 16, 23 and 24 are clear to one skilled in the art and are definite under 35 U.S.C. §112, second paragraph, with respect to the terminology "calculating a root mean square distance (RMSD) between elements corresponding in the first point set of the probe structure and the second point set of the plurality of second subsets of the target structure to automatically determine a distance between the elements of the first point set and the elements of a second point set."

H. The Examiner submitted that claims 16, 23 and 24 are indefinite under 35 U.S.C. §112, second paragraph, with respect to the terminology "a predetermined threshold value."

It is respectfully submitted that determination of "a predetermined threshold value" is described, for example on page 31, lines 17-29:

> A dotted line represents generated candidates for correspondence, and a solid line represents an optimum correspondence (a_1 and b_2, a_2 and b_3, a_3 and b_4) among the generated candidates. In this figure, nil corresponds to a case where no corresponding point exists. By using the nil, an optimum correspondence can be generated even in the case where the number of elements of one set to be related differs from that of the other to be related. An optimum correspondence can be generated by applying Kabsh's method to thus generated combinations, and selecting a combination whose root mean square distance value (r.m.s.d. value) is smallest.

and is further described on page 35, line 31 through page 37, line 19 of the specification:

> (5)   Refining of candidates based on a threshold value condition
>   The point sets can be more efficiently related by setting a specified threshold value in the aforementioned methods (1) to (4), and pruning a retrieval path if an attribute value of a candidate is greater than this threshold value. As this threshold

value, for example, restriction in a nil number (the
number of nil) and restriction in a r.m.s.d. value can
be used.

    (a)   Restriction in a nil number

    When a total number of nil becomes
too large among the generated combinations,
meaningless candidates for combinations are generated
as a result. Accordingly, in relating the elements of
the point sets A and B, if the total number of nil
becomes in excess of a given threshold value, the
generation of the unnecessary candidates can be
prevented by excluding these from the candidates,
thereby relating the elements more efficiently.

    Fig. 21 shows an example of pruning
in a case where a total number of nil is restricted to
0 in relating a point set $A = \{a_1, a_2, a_3\}$ to a point
set $B = \{b_1, b_2, b_3, b_4\}$. In this figure, a portion
designated at x in a tree structure is a portion to be
pruned.

    (b)   Restriction in an r.m.s.d. value

    In the case where an r.m.s.d. value
of all the points related thus far becomes exceedingly
bad by relating an element a_i of a point set A to an
element b_j of a point set B, it is preferable to
exclude this point from consideration of the
candidates. In view of this, the r.m.s.d. value of
all the points when the element a_i is related to the
element b_j is calculated, and this point is selected as
a candidate if the calculated r.m.s.d value is not
greater than a given threshold value. On the
contrary, this point is excluded from the candidates
if the r.m.s.d value is in excess of the given
threshold value. In this way, the candidates for a
point to be related can be generated more efficiently.

    (6)   Refining of candidates based on an
            attribute of a point

> The number of candidates for a point to
> be related can be reduced by using an attribute of the
> point in relating an element a$_i$ of a point set A to an
> element b$_j$ of a point set B. The attributes of the
> point, for example, include the type of an atom, an
> atomic group, and a molecule, the hydrophilic
> property, the hydrophobic property, and the positive
> or negative charge. It is determined whether the
> point is selected as a candidate by checking whether
> these attributes coincide.
>
> For example, in the case of relating
> elements constituting proteins, the number of
> candidates for a point to be related can be reduced by
> using the type of an amino acid residue (corresponding
> to an atomic group) as an attribute of the point.
> Regarding the types of amino acid residues or the
> like, please refer to references such as "Fundamental
> to Biochemistry," pp. 21-26, Tokyo Kagaku Dohjin
> Shuppan.

Hence, it is respectfully submitted that what "a predetermined threshold value is predetermined with respect to is clear to one skilled in the art.

Thus, it is respectfully submitted that claims 16, 23 and 24 are clear to one skilled in the art and are definite under 35 U.S.C. §112, second paragraph, with respect to the terminology "a predetermined threshold value."

I. The Examiner submitted that claims 16, 23 and 24 are indefinite under 35 U.S.C. §112, second paragraph, with respect to the terminology "a character sequence expressing the input amino acid sequence and "a character sequence expressing the amino acid sequence."

ON page 17, line 33 through page 18, line 8, the specification states:

In detecting the length of LCS between the amino acid sequences expressed by a character sequence I and a character sequence II, the LCS detection unit 30 reads the characters individually from the character sequence I and generates an occurrence table indicate of the occurrence positions of the respective characters in the character sequence in the Step I as shown in the processing flow of FIG. 2.

It is respectfully submitted that the terminology "character sequence" is described on page 18, lines 8-20 of the specification:

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        This occurrence table is generated, for example, by
linking array elements P[1] to P[26] corresponding to
alphabets A to Z with data of the occurrence positions of
the respective characters by pointers 62, as shown in Fig.
5.  For instance, in the case where the amino acid sequence
of the character sequence I is expressed as "ABCBDAB," the
occurrence table is generated such that "A" occurs in the
sixth and first places; "B" occurs in the seventh, fourth,
and second places; "C" occurs in the third place; and "D"
occurs in the fifth place.  In Step 1, an array S[i] having
the same size as the character sequence I, which is used in
the subsequent processing, is initialized and a zero value
is set in each entry.
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FIG. 5 also illustrates a character sequence.

Hence, the terminology "character sequence expressing an amino acid sequence" is submitted to be clear to one skilled in the art.

Thus, it is respectfully submitted that claims 16, 23 and 24 are clear to one skilled in the art and are definite under 35 U.S.C. §112, second paragraph, with respect to the terminology ""a character sequence expressing the input amino acid sequence and "a character sequence expressing the amino acid sequence."

It should be noted that claims 17 and 25 are submitted to be allowable under 35 U.S.C. §112, second paragraph, with respect to all of (A)-(I) above for at least the reasons amended claims 17 and 25 are patentable under 35 U.S.C. §112, second paragraph, as described more fully above.

DOUBLE PATENTING:

In the Office Action, at pages 11-13, claims 16, 17, and 23 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 13 of copending Application No. 09/910,071. This rejection is traversed and reconsideration is requested.

Since U.S. Patent Application No. 09/910,071 has not yet been issued as a patent, and since the all of the claims of the instant application have not yet been indicated as allowable except for the provisional rejection, it is believed that any submission of a Terminal Disclaimer or arguments as to the non-obvious nature of the claims would be premature. MPEP 804(I)(B). As such, it is respectfully requested that the applicants be allowed to address any obviousness-type double patenting issues remaining once the rejection of the claims under 35 U.S.C. §101 and

112 is resolved or on allowance of U.S. Patent Application No. 09/910,071.

CONCLUSION:

In accordance with the foregoing, it is respectfully submitted that all outstanding objections and rejections have been overcome and/or rendered moot, and further, that all pending claims patentably distinguish over the prior art. Thus, there being no further outstanding objections or rejections, the application is submitted as being in condition for allowance which action is earnestly solicited.

If the Examiner has any remaining issues to be addressed, it is believed that prosecution can be expedited by the Examiner contacting the undersigned attorney for a telephone interview to discuss resolution of such issues.

If there are any underpayments or overpayments of fees associated with the filing of this Amendment, please charge and/or credit the same to our Deposit Account No. 19-3935.

Respectfully submitted,

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